

### REMARKS

Claims 2, 3, 5, 8, 15, and 16 are pending and at issue in the application.

This response is submitted in accordance with 37 C.F.R. §1.116(a) and §1.116(b) in order to present the rejected claims in a better form for allowance or appeal. The amendment is necessary to eliminate rejections under 35 U.S.C. §103. This amendment was not presented earlier because it was believed, and is still believed, that all outstanding issues were overcome in Amendment "D" filed April 6, 2005. This amendment should be entered because it places the application in better form for allowance or appeal, and the amendment does not require further searching or present any new issues.

Claims 2, 3, 5, 7, 8, 15, and 16 stand rejected under 35 U.S.C. §103 as being obvious over DuBois U.S. Patent No. 6,399,601 ('601) in view of U.S. Patent No. 5,972,342 ('342) and further in view of U.S. Patent No. 5,753,225 ('225). The rejection is based on a contention that the '601 patent teaches a composition containing sildenafil for treating diabetes and diabetic complications. For the reasons previously set forth in Amendment "D" and because the primary '601 reference is an improper reference, it is submitted that this rejection is in error and should be withdrawn.

The examiner's rejection is based primarily on the '601 patent, stating at pages 4 and 5 of the Office Action:

"Du Bois teaches a pharmaceutical composition comprising sildenafil for

the treatment of diabetic complications such as diabetic neuropathy (metabolic neuropathy), and retinopathy. (abstract, column 23, line 63 through column 24, line 39, particularly, column 24, line 38). Du Bois teaches treatment of diabetic complication [sic], such as neuropathy, nephropathy, retinopathy are included in the treatment of diabetes. (column 23, line 67 though [sic] column 24, line 2). Dubois [sic] teaches that sildenafil is a representative agent that can be used to treat diabetes. (column 24, lines 18-39)."; and

"It would have been obvious to one of ordinary skill in the art to employ sildenafil comprising composition taught by Du Bois for the treatment of diabetic neuropathy set forth in claim 5, including peripheral polyneuropathy, paresthesias and autonomous neuropathies and also treat the etiology of peripheral neuropathies including polyneuropathy (toxic neuropathies and metabolic neuropathies) because the specified neuropathies set forth in claim 5 are the various forms of diabetic neuropathies and because Du Bois teaches that the composition comprising sildenafil is useful for the treatment of diabetic neuropathies which encompasses various forms including peripheral polyneuropathy, paresthesias and autonomous neuropathies, and peripheral polyneuropathy which is caused by toxic neuropathies and metabolic neuropathies as taught by Ratsimamanga et al. and Clary et al. respectively. To optimize the amount of sildenafil for the treatment of neuropathies is obvious because Du Bois teaches that sildenafil comprising composition is useful for the treatment of diabetic complications such as diabetic neuropathy encompassing various forms."

The examiner's reliance upon the '601 for a teaching that sildenafil treats diabetes or diabetic neuropathies is misplaced because this disclosure cannot be granted the benefit of the filing date (September 30, 1999) of the provisional application (Serial No. 60/157,148) upon which the '601 patent is based, but rather must be limited to the filing date of the '601 patent. More particularly, for the reasons set forth below, the disclosure relied upon by the examiner has an effective date of September 27, 2000, which is the filing date of the nonprovisional application leading to the '601 patent, rather than the filing date of the provisional application upon which the '601 patent is based, i.e., September 30, 1999. The present application was filed as a PCT application on July 27, 2000. Therefore, the '601 disclosure relating to sildenafil and the treatment of diabetes was made after the filing date of the present application.

Applicant studied the provisional application upon which the '601 patent is based, and especially the portions corresponding to the '601 patent relied upon by the examiner. The examiner relies upon "column 23, line 63 through column 24, line 39, particularly column 24, line 38" of the '601 patent to support the rejection. The most relevant portion of the '601 patent relied upon by the examiner states (emphasis added):

"Representative agents that can be used to treat diabetes include . . . phosphodiesterase inhibitors, both cAMP and cGMP type: sildenafil, L66398: L-386,398;"

The corresponding disclosure in the provisional application upon which the '601 patent is based is different, however. The corresponding disclosure, at page 33, line 10 of the provisional application states:

"phosphodiesterase inhibitors:  
L-386,3908."

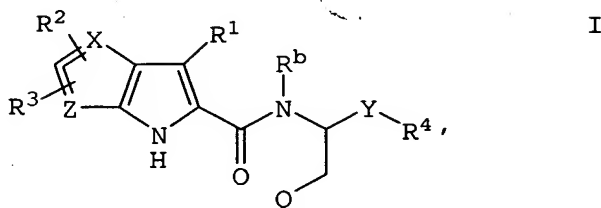
A copy of page 33 from U.S. provisional application 60/157,148 ('148 application) is submitted concurrently with this response as Exhibit A for the convenience of the examiner.

This disclosure from the provisional '148 application not only fails to disclose sildenafil, but it also apparently fails to disclose cGMP-type phosphodiesterase inhibitors. The L-386,398 inhibitor disclosed in the provisional application apparently is a PARP inhibitor with some activity against phosphodiesterases. See attached Exhibit B, which includes the results of a search directed to L-386,398. Therefore, the *first* disclosure of a cGMP phosphodiesterase inhibitor in general, and sildenafil in particular, is in the *nonprovisional* application leading to the '601 patent, having a filing date of September 27, 2000, which is *after* the effective filing date of the present application (July 27, 2000). The portions of the '601 patent relied upon by the examiner to support the rejection, therefore, are not citable against the present claims.

The examiner also incorrectly relies upon the abstract of the '601 patent to support the rejection. The '601 abstract, in its entirety, states:

"ABSTRACT

This invention relates to compounds of Formula I



or stereoisomers, pharmaceutically acceptable salts or prodrugs thereof or a pharmaceutically acceptable salts [sic] of the prodrugs. This invention also relates to pharmaceutical compositions comprising a compound of Formula I, and to methods of treatment of diabetes, insulin resistance, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, cataracts, hyperglycemia, hypercholesterolemia, hypertension, hypeninsulinemia, hyperlipidemia, atherosclerosis, or tissues ischemia."

The abstract absolutely fails to teach or suggest sildenafil, or any other phosphodiesterase inhibitor, to treat any condition. The abstract is limited to a disclosure of a compound of Formula I, its compositions, and to methods of treating diseases.

Because the '601 patent teachings arguably relevant with respect to the present claims either are not citable against the present claims and/or fail to teach or suggest using sildenafil to treat any condition, it is submitted that the rejection of claims 2, 3, 5, 7, 8, 15, and 16 under 35 U.S.C. §103 should be withdrawn. The secondary and tertiary references, in the absence of the primary '601 reference, cannot support the examiner's obviousness rejection.

Furthermore, applicants further submit that the '601 patent should be eliminated as a reference in its entirety. The '601 patent is granted the benefit of a September 30, 1999 filing date for all information included in provisional U.S. patent application Serial No. 60/157,148. The enclosed Declaration of Juerg Lareida establishes that the presently claimed invention was conceived and reduced to practice prior to the earliest filing date of the '601 patent. Accordingly, even if the entire '601 patent disclosure is granted the benefit of a September 30, 1999 filing date, the '601 patent still is not available as a reference against the present claims.

For all the reasons set forth above, it is submitted that the rejection of claims 2, 3, 5, 7, and 8, 15, and 16 as being obvious over cited '601, '342, and '225 patents should be withdrawn. The disclosure of the '601 patent is not available as a reference against the present claims for each of the reasons stated above and in the Declaration of Juerg Lareida, and the remaining '342 and '225 patents, cannot support an obviousness rejection of the present claims in the absence of the '601 patent. Furthermore, even if the '601 patent was available as a reference, the present claims would not have been obvious over the combined teachings of the '601, '342, and '225 patents for the reasons set forth in Amendment "D" and prior amendments.

In summary, it is submitted that all pending claims are in a form and scope for allowance. An early

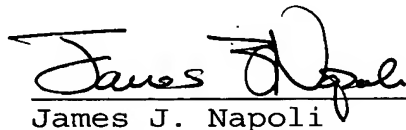
and favorable action on the merits is respectfully requested.

Should the examiner wish to discuss the foregoing, or any matter of form in an effort to advance this application toward allowance, the examiner is urged to telephone the undersigned at the indicated number.

Respectfully submitted,

**MARSHALL, GERSTEIN & BORUN LLP**

By

A handwritten signature in dark ink, appearing to read "James J. Napoli", is written over a horizontal line.

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